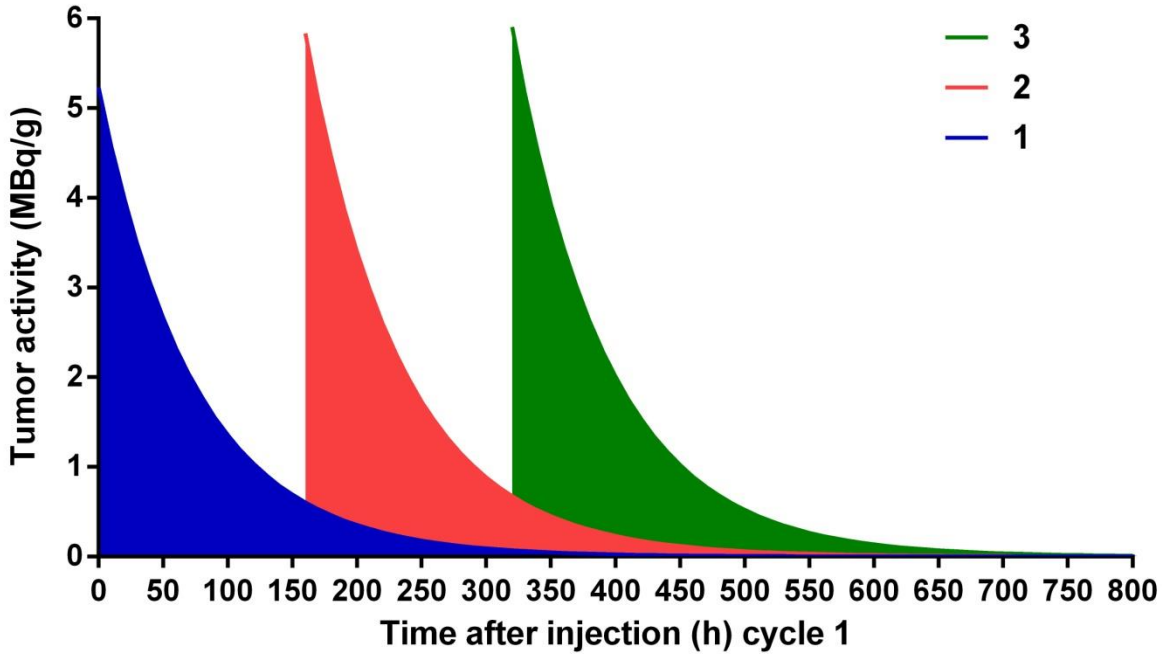
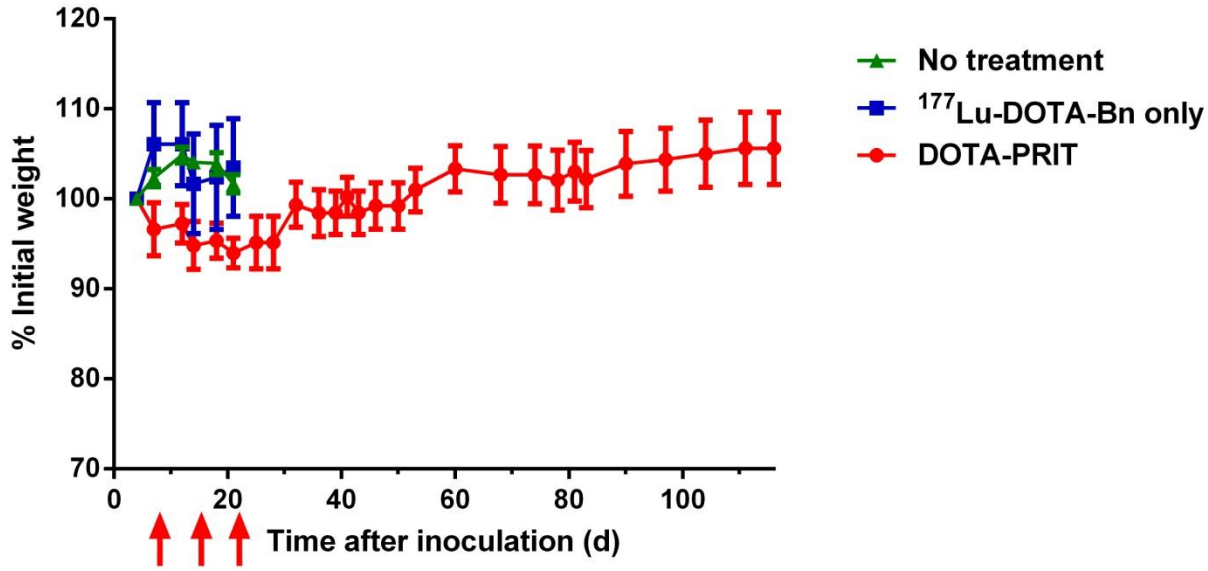
Supplemental Data



SUPPLEMENTAL FIGURE 1. Representative sample of simulated three-cycle treatment curves. This was the approach used in prior studies, but it does not capture tumor dose density distribution as adequately as direct measurement during all cycles.



SUPPLEMENTAL FIGURE 2. Animal weight plotted as the percent of baseline from day 4 after tumor inoculation.

	Cycle 1		Cycle 2		Cycle 3	
Mouse	Dose 0-160 h (Gy)	Cumulated dose (Gy)	Dose 160-320 h (Gy)	Cumulated dose (Gy)	Dose 320-∞ (Gy)	Cumulated dose (Gy)
1	29.1	32.8	32.4	65.8	37.1	98.7
2	21.7	24.8	24.4	49.6	28.3	74.4
3	25.9	36.1	33.2	72.2	49.3	108
4	19.9	24.5	23.6	49.0	29.8	73.5
5	33.4	35.8	35.6	71.6	38.4	107
Mean	26.0	**30.8**	29.9	**61.6**	36.6	**92.3**
SD	5.5	**5.8**	5.5	**11.5**	8.4	**17.2**
CoV	21%	19%	18%	19%	23%	19%

Cycle 2 and cycle 3 data were simulated using the estimated effective half-life from the exponential fit of cycle 1 data. Doses were extrapolated out to infinity, taking into account residual activity from each previous cycle. The simulation shows expected doses for each cycle assuming the same elimination kinetics as in cycle 1 with only one injection.

SUPPLEMENTAL TABLE 1. Mean radiation-absorbed doses to xenografts based on simulated three-cycle treatment.

	Normal[a] (n = 10)	Normal[b] (n = 3)	Day 100 post-treatment (n = 5)	Day 180 post-treatment (n = 1)[c]	Day 200 post-treatment (n = 3)
Hematology					
WBC (K/uL)	2.6 ± 1.0	4.5 ± 0.8	7.41 ± 2.23	6.67	7.41 ± 4.31
RBC (M/uL)	8.2 ± 0.5	9.0 ± 0.7	8.76 ± 0.34	13.59	9.38 ± 0.18
Hemoglobin (g/dL)	15.0 ± 0.7	14.4 ± 0.3	13.7 ± 0.43	20.5	14.37 ± 0.85
Platelets (K/uL)	1099.6 ± 142.8	911.7 ± 86.3	819.0 ± 118.6	250	882.0 ± 162.5
Lymphocytes (K/uL)	N/A	2.75 ± 0.53	4.44 ± 2.11	2.52	4.14 ± 1.86
Neutrophils (K/uL)	N/A	1.33 ± 0.32	2.35 ± 0.54	3.93	2.07 ± 1.28
Monocytes (K/uL)	N/A	0.31 ± 0.15	0.39 ± 0.17	0.13	0.877 ± 1.07
Clinical Chemistry					
BUN (mg/dL)	30.4 ± 2.6	24.7 ± 1.2	36.4 ± 2.51	41	34.3 ± 4.5
CREA (mg/dL)	0.3 ± 0.0	0.197 ± 0.015	0.256 ± 0.013	below 0.2*	0.163 ± 0.021
ALT (U/L)	33.4 ± 5.2	37.0 ± 8.0	37.4 ± 10.1	56	65.3 ± 37.6
AST (U/L)	110.5 ± 19.3	74.3 ± 9.1	78.0 ± 11.1	114	126.3 ± 38.4
ALP (U/L)	87.5 ± 11.7	113.0 ± 21.7	82.6 ± 7.2	182	78.3 ± 6.1

Data is provided as mean ± SD. Note: reference ranges used for hematology and serum chemistry are typically defined as mean ± 2SD.

N/A = not available, WBC = white blood cells, BUN = blood urea nitrogen, CREA = creatinine, ALT = alanine aminotransferase, and AST = aspartate aminotransferase.

[a]Data from Harlan Laboratories, Athymic Nude, Hsd: Athymic Nude-*Foxn1*^{nu}, 16 to 17-week-old females.

[b]Harlan Laboratories, Athymic Nude, Hsd: Athymic Nude-*Foxn1*^{nu}, ~9-month-old females.

*The lower limit of linearity for CREA is 0.20 mg/dL.

[c]Mouse was moribund at time of necropsy submission.

SUPPLEMENTAL TABLE 2. Select hematological and clinical chemistry analyses of athymic female nude mice bearing s.c. SW1222 tumors following DOTA-PRIT therapy with huA33-C825, CA, and 167 MBq total of ^{177}Lu-DOTA-Bn at days 100 (n = 5), 180 (n = 1), and 200 (n = 3) post-treatment. All other hematology and clinical chemistry data not listed is available upon request.

Organ	Histopathology	Study endpoint and incidence (number of mice with events/number of mice examined)		
		96 days post-treatment (n = 5)	158 days post-treatment (n = 1)*	200 days post-treatment (n = 3)
Liver	Extramedullary hematopoiesis (mild)	1/5		
	Perivascular lymphoid infiltrate, focal (mild)	1/5		
	Hepatitis (moderate), granulomatous and eosinophilic, with hepatocellular necrosis, multifocal random			1/3
	Epithelial hyalinosis with mild lymphoplasmacytic mucosal infiltrate, multifocal			1/3
	Hepatitis (mild), histiocytic and eosinophilic, multifocal, random			1/3
	Minimal centrilobular hepatic lipidosis with rare hepatocellular apoptosis, multifocal		1/1	
Spleen	Lymphoid hyperplasia (mild); no splenic white pulp	1/5		
	Lymphoid hyperplasia (mild); splenic white pulp prominent	1/5		
	Lymphoid hyperplasia (moderate); splenic white pulp prominent	1/5		
	Splenitis, granulomatous and eosinophilic, multifocal (moderate)			1/3
	Follicular lymphoid hyperplasia			1/3
	Erythroid hematopoietic hyperplasia (moderate)		1/1	
Kidney	Multifocal hyaline glomerulopathy (moderate; confirmed with positive PAS and negative Congo red staining)	1/5		
	Medullary tubular ectasia, multifocal, minimal, with luminal protein	1/5		
	Minimal tubular degeneration, multifocal, unilateral			1/3
Inguinal lymph node	Lymphoid hyperplasia (mild)	2/5		
	Lymphoid hyperplasia (moderate)	1/5		

SUPPLEMENTAL TABLE 3. Summary of histopathologic observations of 9 SW1222 tumor-bearing mice that were treated with DOTA-PRIT, 96-200 days post-treatment (total ^{177}Lu-DOTA-Bn administered activity: 165 MBq).

*Note: This mouse required sacrifice due to poor body condition and low body weight (>25%). Additional findings included: *lungs*: marked interstitial fibrosis, with moderate alveolar histiocytosis, multifocal, chronic; *heart*: marked right ventricular myocardial hypertrophy and moderate focal pericarditis, histocytic, with fibrosis, chronic.